REMARKS

With this response, Applicants have amended claims 2, 4, 6, 14, 18, 23, 29, 30, 35, 37, and 39, and have cancelled claims 22 and 28. . Applicants reserve the right, however, to pursue the subject matter of these claims in any continuation or divisional applications. In view of the arguments provided below and the amendments presented above, Applicants respectfully submit that the Application is now in condition for allowance.

I. Restriction Requirement:

Applicants hereby affirm the election of **Group I**, without traverse, which includes claims 1-18, drawn to compound and pharmaceutical compositions of formula IIc classified in class 544, subclass 278, 279, and 284.

Pending the allowance of claims 1-18, Applicants request the rejoinder of originally filed claims 19 through 39, pursuant to MPEP §821.04. Specifically, Applicants request that the process claims that depend from or otherwise include all the limitations of the patentable product be entered. In anticipation of said rejoinder, and to expedite the prosecution process, Applicants have also amended and/or cancelled certain of these claims 19 through 39.

II. Specification:

The Examiner has objected to the disclosure and states that some species of formula IIc on page 254-282 (e.g., Examples 82, 85-89, 99-101, etc.) are not analogous to the product obtained from Method A and states that the discrepancy causes confusion to one skilled in the art.

Applicants respectfully disagree with the Examiner and respectfully submit that a chemist of ordinary skill in the art would recognize that Method A is merely a representative example and that the preparation of the species described in the Examples would require using the appropriate amine to displace the chloro group in the chloropyrimidine with $Q\text{-}R^1$. Applicants would also like to direct the Examiner's attention to **Scheme I** on page 211 where general conditions for the synthesis of compounds of the invention are described. In particular, on page 211, line 14, a reference is provided that describes the conditions used for the displacement of the chloro group of intermediate **3** by $Q\text{-}R^1$, for the preparation of compounds where Q is an N-

link, and where R^1 is T-(Ring D). Applicants respectfully submit that in view of the general description and Scheme provided on page 211, coupled with the knowledge available to the chemist of ordinary skill in the art (specifically, a chemist of ordinary skill in the art would recognize the need to use the appropriate amine to displace the choro group to arrive at the desired product), the disclosure would not cause confusion to a chemist of ordinary skill in the art.

III. Rejection under 35 U.S.C. §112, second paragraph:

a. The Examiner has rejected claim 14 and states that there is insufficient antecedent basis for the limitation of "benzo" in the claim. In response to the Examiner's rejection, Applicants have amended claim 14 to exclude "benzo" (since as the Examiner has pointed out, claims 12 has already excluded "benzo"). Applicants thus respectfully request that the rejection of claim 14 be withdrawn.

b. The Examiner has rejected claim 18 and states that it is unclear if the additional agent is in the same formulation with the compound or if it is in a separate formulation. In response to the Examiner's rejection, Applicants have amended claim 18 to clarify that the additional agent is in the same formulation with the compound. Applicants thus respectfully request that the rejection of claim 18 be withdrawn.

IV. Rejection under 35 U.S.C. §112, first paragraph:

The Examiner has rejected claims 1, 2, 4, 6, and 8-18, and states that the specification, while being enabling for the preparation, and use of compounds and compositions of formula IIc with ring D as an aryl ring (i.e., phenyl or substituted phenyl), does not reasonably provide enablement for the preparation and use of compounds and compositions of formula IIc with ring D as a heteroaryl or heterocyclyl ring. Specifically the Examiner states that the specification only describes Method A for compounds of formula IIc on page 217, and that said method only discloses 3-chloro-aniline as the starting material corresponding to $-NHR^1$ or NH-(ring D), and that no other starting material is disclosed for ring D as a heteroaryl or heterocyclyl ring in formula IIc. The Examiner also states that although the teaching of Mederski *et al.* describes the preparation of a few quinazolinyl compounds with indolyl-amine, or pyridyl-amine at the second position, said compounds differ from the claimed compounds by not having pyrazolyl-amine at

the fourth position, and therefore the skilled chemist cannot assume the same course of reaction to obtain the claimed compounds.

Applicants respectfully disagree with the Examiner and submit that claims 1, 2, 4, 6, and 8-18 are indeed enabled because 1) the starting materials utilized for the preparation of compounds where R^1 is heteroaryl or heterocyclyl are commercially available; 2) Applicants have provided sufficient guidance for the synthesis of compounds substituted with $-NHR^1$ in the 2-position of the pyrimidine and simultaneously substituted with amino-pyrazole in the 4-position (see, pages 211 through 214 in the specification, and Examples 82, 86, 88, 89, 99, 101, 111, 114, 116, 117, 132, 148, and 159); and 3) there is significant guidance in the art, in addition to references specifically cited in the specification, for the synthesis of compounds substituted by $-NHR^1$ in the 2-position of the pyrimidine.

Applicants would also like to point out that they are not relying on the teaching of Mederski *et al.* to satisfy their enablement requirement. Rather, Applicants respectfully assert that sufficient guidance (including specific examples) has been provided in the specification, which, in combination with methods and materials known and readily available to a chemist of ordinary skill in the art (many of which are specifically cited in the specification), is sufficient to enable one of ordinary skill in the art to practice the invention without undue experimentation.

Specifically, in response to the Examiner's rejection (and assertion that the specification only Method A for compounds of formula IIc on page 217 is provided), Applicants would like to direct the Examiner's attention to the specification, pages 211 through 214, where general methods for the preparation of 4-aminopyrazole compounds where Q is NH are described and depicted (and additionally cite known methods in the art). The procedure described in Method A is clearly based upon these general methods and the methods known in the art and, as articulated above in response to the rejection under § 112, second paragraph, one of ordinary skill in the art would immediately recognize the necessity of using the appropriate amine for reaction with the chloropyrimidine to obtain a desired product. In response to the Examiner's assertion that one skilled in the art would have to carry out undue experimentation to make and use compounds and compositions of formula IIc with ring D as a heteroaryl or heterocyclyl ring, Applicants would also like to direct the Examiner's attention to Examples 82, 86, 88, 89, 99, 101, 111, 114, 116, 117, 132, 148, and 159 in the specification describing the synthesis and spectral data for compounds where QR^1 is -NH(heteroaryl), or –NH(heteroaralkyl). Although these Examples

refer back to Method A, Applicants would like to reiterate their point that one of oridinary skill in the art, in view of the knowledge generally available to one of skill in the art, would understand the necessity of using the appropriate amine in the reaction procedure (in place of 3-chloro-aniline). In response to the Examiner's assertion that references or descriptions for the synthesis of specific starting materials have not been provided (specifically for indolyl-amine or pyridyl-amine referring to the Mederski reference), Applicants would like to point out that these amines (as well as many others) are actually commercially available (*see*, for example, Aldrich Catalog Handbook of Fine Chemicals). The courts have pointed out that "[n]ot every last detail [of an invention need] be described [in a patent specification], else patent specifications would turn into production specifications, which they were never intended to be." *In re Gay*, 309 F.2d 769, 774, 135 U.S.P.Q. 311, 316 (C.C.P.A. 1962). Additionally, it has been stated that "the law does not require a specification to be a blueprint in order to satisfy the requirement for enablement under 35 U.S.C. § 112, first paragraph," *Staehelin v. Secher*, 24 U.S.P.Q.2d 1513, 1516 (Bd. Pat. App.& Int. 1992). It has also been stated that a specification need not describe--and best omits--that which is well-known in the art. *See, e.g., In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991). Applicants respectfully submit that compounds (for example the heteroaryl amines described above and others) that are sold by Sigma-Aldrich and are published in the Aldrich Catalog are indeed well known and readily available to a chemist of ordinary skill in the art.

Accordingly, Applicants respectfully submit that the availability of these starting materials to one of ordinary skill in the art, coupled with the guidance generally available in the art and specifically provided in the schemes, description, and Examples (including references to procedures available in the art, see pages 211 through 214) is sufficient to satisfy the enablement requirement for the full scope of claims 1, 2, 4, 6, and 8-18. Applicants thus respectfully request that the Examiner withdraw the rejection of claims 1, 2, 4, 6, and 8-18.

V. Claim Objections:

The Examiner has objected to claim 3, 5, and 7 under 37 CFR § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicants have amended claims 2, 4, and 6 to further clarify that, in each of claims 2, 4, 6, *one or more of the compound variables* (and possibly, *but not necessarily,* all of the compound

variables) are selected from the listed group. In contrast, claims 3, 5, and 7 require that *all* of the compound variables are chosen from the specifically listed group, and thus claims 3, 5, and 7 are indeed a subset of claims 2, 4, and 6, respectively, where all of the compound variables are selected from the listed group. In view of the clarification to claims 2, 4, and 6, Applicants respectfully request that the Examiner withdraw the rejection of claims 3, 5, and 7.

CONCLUSION

In view of the arguments presented above, and the amendment of claims 2, 4, 6, 14, 18, 23, 29, 30, 35, 37, and 39, and the cancellation of claims 22 and 28, Applicants believe that the present Application is currently in condition for allowance. Applicants would like to thank the Examiner for careful review of this application. If it is believed that a telephone call would expedite prosecution, the Examiner is invited to contact the undersigned at (617) 444-6536. The Commissioner is authorized to charge any fees (or credit any overpayments) to Deposit Account Number: 50-0725, reference number VPI/00-130-2 US.

Respectfully submitted,

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